REPLICATIVE-FORM OF POLY(TRIOSE-PHOSPHATE)

by

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Summary. Pathway invariants and other evidence led to the conclusion that poly(triose-phosphate) replication preceded appearance of RNA. Macromolecular replication and the pathways of central metabolism thus evolved simultaneously. These findings offer a resolution to a long-standing issue regarding prebiotic evolution and a new paradigm for explaining the origin of life.

Amino acid synthesis pathways have revealed much about the formation of the genetic code, in the interval preceding the Last Common Ancestor (LCA) more than 3.5 billion years ago (Davis, 1999, 2008, 2009). It is notable, for example, that almost all intermediates in these pathways bear a free α-carboxyl. The ubiquity of this group among amino acid intermediates points to masking by a tRNA cofactor during the growth of these pathways. More broadly, this 'invariant' of amino acid synthesis pathways conforms with the proposition that tRNA diversification coordinated formation of the genetic code with the growth of amino acid synthesis pathways. In this connection, amino acids synthesized from the same precursor generally have adaptor molecules cognate with nearest-neighbor codons. Pre-LCA tRNA paralogs for same-family amino acids also contain related base sequences, revealing they had diversified from a common ancestral tRNA species (Davis, 2008).

A free α-carboxyl is also an invariant of the citrate cycle. Since the pathways for most amino acids incorporated into proteins originate at branch reactions in this cycle, tRNA-like cofactors plausibly participated in the pre-LCA citrate cycle (Davis, 1999). This implicates RNA in coordinating and catalyzing the citrate cycle, in accord with the apparent implausibility of stand-alone metabolic cycles in the prebiotic era (Orgel, 2008). Beyond the citrate cycle lays the central trunk with its phosphorylated trioses. It terminates with glyceraldehyde-3-phosphate and dihyroxyacetone-phosphate combining to form the hexose, D-fructose-1,6-phosphate. Glyceraldehyde-3-phosphate and dihydroxyacetone-phosphate are both phosphorylated components of the formose cycle. The formose cycle spontaneously and autocatalytically converts a 1-carbon source (formaldehyde) to glycoaldehyde, by cleaving an aldotetrose in a retroaldol reaction

(Breslow, 1959). Consistent with being a primitive process, unaided by a macromolecular scaffold, or cofactors, no invariant site occurs in the formose cycle. The diphosphorylated hexose produced by formose cycle derivatives glyceraldehyde-3-phosphate and dihydroxyacetone-phosphate, on the other hand, contributes to ribulose-5-phosphate formation in the pentose cycle and all its components (mono- and di-phosphorylated fructose, xyulose-5-phosphate, mono- and di-phosphorylated ribulose, mono- and di-phosphorylated glycerate, glyceraldehyde-3-phosphate, and dihydroxyacetone-phosphate) contain a terminal phosphate. This is indicative of forming a polyphosphate scaffold, based on analogous features noted in amino acid synthesis pathways, substantiated by code structure and pre-LCA tRNA phylogenetics (Davis, 2008). A second noteworthy feature of the pentose cycle is the carboxylation of D-ribulose-1,5-phosphate at C2. This step follows the phosphorylation of ribulose-5-phosphate and evident formation of a second polyphosphate scaffold. Cleavage of ribulose-1,5-phosphate at its C2-C3 bond, in a retroaldol reaction, then produces two separate poly(3-P-D-glycerate) molecules. From this perspective, the pentose phosphate cycle conserves evidence of pre-RNA replication. The replicative-form of poly(triose-phosphate), poly(ribulose-1,5-phosphate-2-carboxylate), is depicted in Fig. 1.

This finding shows metabolism and macromolecular replication arose simultaneously, long before appearance of the first polynucleotide, a proto-RNA. Reconstructing from the pathway evidence, it appears formose cycle components, glyceraldehyde and tautomer, dihydroxyacetone, produced at a site such as an alkaline thermal vent, reacted with surface-bound inorganic polyphosphate molecules. Thermodynamic forces and population dynamics would drive evolution toward an efficient self-replicating polymer

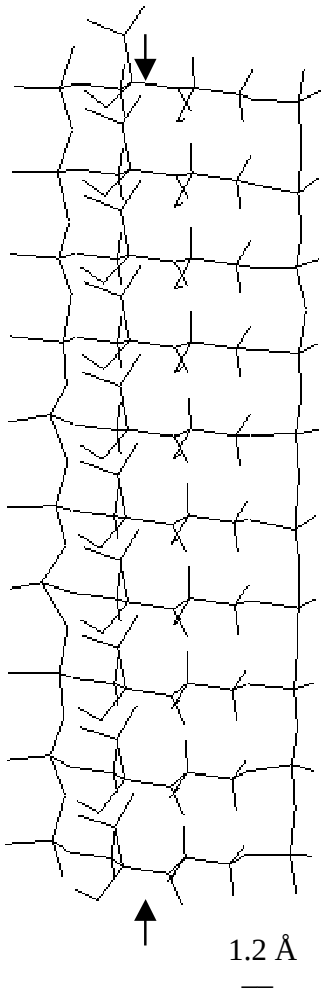

Figure 1. Replicative-form of poly(triose-phosphate). Two vertical polyphosphate strands (8.2 Å apart) of a 10-mer, crosslinked by D-ribulose-2-carboxylate (triose dimer) molecules spaced at 2.9 Å are shown. The C2-C3 bond (numbered left to right, indicated by arrows) is split in a reverse aldol reaction, producing two poly(triose-phosphate) strands. Bond lengths and angles were obtained from Levitt (1983) and Pauling (1960) and constructed with Facio 16.4.1 molecular model building software.

such as the linear double-stranded poly(triose-phosphate) molecule (PTP) depicted in Fig. 1. PTP can form with either D, or L, optical isomers, but not both. Steric hinderance between cross-chiral monomers prevents stacking within the polymer. Since the pentose cycle contributes D-ribose-5-phosphate to RNA synthesis, the chiral specificity required for double helix formation (Joyce et al, 1989) can be traced to PTP. On the other hand, double helix formation is not constrained to ribose bearing a furanose ring (Eschenmoser, 1999). This restriction can reasonably be linked to the early reliance on a single source of phosphorylated sugar - cyclization of ribulose-5-phosphate.

PTP can form extended and contracted configurations. Cleavage of a phosphate bond may allow movement between both. As optically pure monomers can be arranged in a 5 → 1, as in Fig. 1, or 1 → 5, in double-stranded PTP. The potential for evolving complex sequences appears non-existent, however, as replication produces two homologous single-strand PTP molecules, all sequence complexity is lost. With pentose cycle growth oriented 5 → 1, the complexity of an aperiodic double-stranded PTP molecule could be expressed by cross-linking neighboring poly(P) strands, to form a distinct sheet pattern. The resulting mono-molecular sheets conceivably provided the membrane of the first protocell. A 3-dimensional cross-linking pattern could form a triose-phosphate gel. The catalytic activity of PTP molecules (triozymes) clearly merits investigation. Issues related to coding capacity and catalytic potential apparently drove the transition from PTP to RNA based life-forms, encapsulated by the first coenzyme A synthesized lipids.

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